



Attorney's Docket No.: 07917-178001 / UMMC 03-14

THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Jones et al.
Serial No. : 10/719,054
Filed : November 20, 2003
Title : DIAGNOSING AND TREATING HEMATOPOIETIC CANCERS

Art Unit : 1632
Examiner : Magdalene K. Sgagias
Conf. No. : 3347

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF STEPHEN N. JONES, PH.D.

I, Stephen N. Jones, hereby declare as follows:

1. I am a named inventor on the present application (USSN 10/719,054). I am also an employee of the assignee, the University of Massachusetts Medical School. My present title is Associate Professor in the Departments of Cell Biology and Cancer Biology. A copy of my curriculum vitae is attached hereto as Exhibit A.
2. I have reviewed the Office Action mailed October 5, 2006, and am familiar with the rejections contained therein. In particular, I note that the Examiner alleges that the claims lack enabling support in the application; namely, that we did not demonstrate expression of Wnt5a in a number of blood cell types transduced with Wnt5a *in vitro*, and whether said cells when transferred into a subject would produce therapeutic levels of Wnt5a. I respectfully disagree.
3. The application itself presents the results of experiments that involved transducing two separate B cell lines with a retroviral construct that includes a Wnt5a coding sequence. Page 49, line 20 to page 50, line 7, of the application describes experiments in which 7C6 and 1-8 B cells, which are Abelson leukemia virus-transformed B cells lines that lack Wnt5a expression, were transformed with a retroviral construct encoding Wnt5a. Figure 21 of the application shows Wnt5a expression only in those cells transduced with the Wnt5a vector, and none in those cells transduced with an empty vector. These results clearly demonstrate expression of Wnt5a in transduced blood cells.

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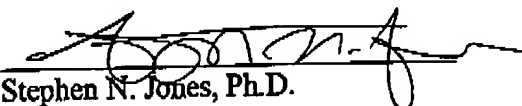
4. As is also demonstrated in Figure 21, cyclin D levels were greatly reduced in those cells transduced with the Wnt5a virus. Cyclin D levels correspond with cell proliferation, thus a decrease in Cyclin D is associated with a decrease in cell proliferation. This is demonstrated in Figure 23, which shows a decrease in BrdU uptake in cells transduced with the Wnt5a virus. Reduced BrdU uptake indicates reduced cell proliferation, thus, expression of Wnt5a by transduced cells results in the desired pharmacological outcome: suppression of proliferation.
5. These cell lines are derived from B cells and are widely accepted models of leukemic cells, and, like the blood cells of the patients with B cell lymphoma described in Example 10 (see pages 51-53) of the present application, lack Wnt5a. The experiments in the present specification demonstrate that expression of Wnt5a in B cells results in a decrease in cell proliferation.
6. In addition, I and the other co-inventors ectopically expressed Wnt5a in NFC cells, a CD4+8+ T cell line that lack endogenous Wnt5a expression (see Figure A of Exhibit B, attached hereto). NFC-WNT5a cells grew significantly slower in culture than NFC cells transduced with control empty vector (see Figure B of Exhibit B). Expression of exogenous Wnt5a also suppressed the level of Cyclin D1 in NFC cells, confirming that Wnt5a can potentially regulate cell cycle progression of DP thymocytes (Figure C of Exhibit B). Furthermore, the level of apoptosis following serum withdrawal was elevated in cells expressing Wnt5a relative to the levels of apoptosis in control NFC cells (Figure D of Exhibit B). Finally, transduction of Wnt5a upregulated levels of the proapoptotic protein Bax, (Figure E of Exhibit B) concomitant with a 4-fold increase in Bax gene expression (Figure F of Exhibit B), confirming that Wnt5a is pro-apoptotic in thymocytes.
7. These results indicate that Wnt5a inhibits the proliferation of cells from different hematopoietic compartments: T cells and B cells, and thus can be expected to be useful in inhibiting proliferation of hematopoietic cancers associated with aberrant proliferation of those cells, i.e., leukemia and non-Hodgkin's lymphoma.

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, under Title 18 § 1001 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

4-2-07
Date


Stephen N. Jones, Ph.D.

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CURRICULUM VITAE

Stephen Nelson Jones, Ph.D.

Associate Professor of Cell Biology and Cancer Biology
University of Massachusetts Medical Center
55 Lake Avenue North
Worcester, MA 01655
(508) 856-7500 (voice) / (508) 856-7510 (fax)
stephen.jones@umassmed.edu

Personal

Born March 1, 1960, in Washington, D.C.
Married: Elizabeth Niedbala, MSW.
Two children: Danielle and Gregory

Education

| | |
|-------------|--|
| 1978 - 1982 | University of Virginia College of Arts and Sciences Charlottesville, Virginia B.A. - Biology |
| 1982 - 1987 | Vanderbilt University School of Medicine Department of Microbiology Nashville, Tennessee Ph.D. - Microbiology Thesis Title - Autoregulation of the Adenovirus E1A Gene |

Professional Experience

| | |
|--------------|--|
| 1998-1992 | Postdoctoral fellow, laboratory of C. Thomas Caskey, M.D., Baylor College of Medicine, Houston, TX |
| 1992-1997 | Postdoctoral fellow, laboratory of Allan Bradley, Ph.D., Baylor College of Medicine, Houston, TX |
| 1997-present | Assistant Professor of Cell Biology, University of Massachusetts Medical School, Worcester, MA |
| 1998-present | Director, Transgenic Animal Modeling Core (Transgenic-Knockout Animal Facility and Gene Targeting Facility), University of Massachusetts Medical School, Worcester, MA |
| 1998-present | Member, UMASS Diabetes and Endocrinology Research Center |
| 1998-present | Member, UMASS Cancer Center |
| 2001-present | Member, Interdisciplinary Graduate Program (IGP) |
| 2003-present | Secondary appointment to faculty in Department of Cancer Biology |
| 2004-present | Associate Professor of Cell Biology, University of Massachusetts Medical School, Worcester, MA |

Honors and Awards

| | |
|-----------|---|
| 1982-1984 | National Cancer Institute Trainee |
| 1987-1988 | National Institute of General Medical Science Trainee |
| 1988-1990 | NIH- National Research Service Award |
| 1996-1997 | Baylor College of Medicine- Postdoctoral Research Award |
| 1999 | Worcester Foundation Trustees Award |

Major Research Interests

Regulation of cell differentiation, proliferation, and tumor suppression.
Mouse modeling of human genetic disorders.

Invited Seminar Presentations

| | | |
|----------|--|-----------------------------------|
| Apr 1997 | Dept. of Medical Genetics | Oregon Health Sciences Inst., OR |
| Oct 1997 | UMASS Research Symposia | Woods Hole, MA |
| Sep 1998 | McArdle Lab Colloquium | University of Wisconsin, WI |
| Nov 1998 | UMASS Research Symposia | Woods Hole, MA |
| Jan 1999 | Dept. of Microbiology | Dartmouth Medical Center |
| Mar 2000 | Graduate Program Seminar | Univ. of Massachusetts, Amherst |
| Jun 2000 | Dept. Molecular Virology | Baylor College of Medicine |
| Oct 2000 | Dept. Human Genetics | Univ. of Michigan Medical School |
| Oct 2001 | ASBMR National Meeting | Phoenix, Arizona |
| Nov 2001 | 1 st Internat. MDM2 Workshop | Univ. of Dundee, Scotland |
| Mar 2002 | Division of Neuropharmacology | Purdue BioPharma, Cranbury, NJ. |
| Mar 2002 | AACR National Meeting | San Francisco, CA |
| Apr 2002 | Fels Institute for Cancer Res. | Temple University, Philadelphia |
| Nov 2002 | Department of Cell Biology | UMASS, Worcester, MA |
| Jan 2003 | Dept of Biological Sciences | Univ. of Tennessee, Knoxville, TN |
| Oct 2003 | 2nd Internat. MDM2 Workshop | Washington, DC |
| Jan 2004 | Ruttenberg Cancer Center | Mount Sinai Med. School, NY |
| Feb 2004 | Mouse Models of Human Disease | Keystone Symposia, Keystone, CO |
| Mar 2004 | Dept of Micro & Immunology | Univ. of Miami School of Med., FL |
| Feb 2005 | Eppley Cancer Institute | U. Neb. Med School, Omaha, NE |
| Mar 2005 | Dept Veterinary Sciences | Univ. of Massachusetts, Amherst |
| Sep 2005 | 3rd Internat. MDM2 Workshop | Konstanz, Germany |
| Jan 2006 | NE Hemat. Malign. Workshop | Worcester, MA |
| Mar 2006 | Dept. Molecular Virology | Baylor College of Medicine |
| Apr 2006 | Symp. Chair- AACR Natl Meet. | Washington. DC |
| Jun 2006 | Department of Medicine | Georgetown University, Wash D.C. |
| Sep 2007 | Organizer: 4th International MDM2 Workshop- | Woods Hole, MA |

Scientific Review

Consultant, Dartmouth Medical Center Transgenic Animal Facility: 1999-2001.
Member, University of California Tobacco-Related Disease Research Study
Section: 2000, 2001.
Member, Visiting Committee on Animal Care and Use, University of
Massachusetts, Amherst: 2000.
Member, Fuller Fellowship Selection Committee, American Cancer Society: 2002.
NIH Special Review Panel- NIAMS study section- 2003
NIH Development-2 Scientific Review Panel (Ad Hoc member)- 2004
NIH External Review Panel- RAND Program award - 2005
Ad hoc reviewer for manuscripts submitted to Molecular and Cellular Biology,
Cell Growth and Diff, Inter J. Cancer, J. Cell Physiology, Oncogene,
Nucleic Acids Res., J. Cell Biochemistry, EMBO, Cancer Research,
Nature, Cancer Cell, Development, and Genes & Development.
Member, Editorial Board, Journal of Cellular Physiology, 2003-present.
External Judge, 2006 Charles Hufnagel Research Forum, Georgetown University

Teaching

Cell Biology 700: Advanced Topics: Experimental Approaches to Gene Therapy.
Course Organizer and Lecturer. Spring 1998.
Interdisciplinary: Genetic Systems- Mammals 1 and 2. Lecturer and discussion
leader. Spring 1998, Spring 1999.
Pharmacology 740: Advanced Topics: Signal Transduction. Lecturer. Fall 1998.
Med. Sciences 600: Graduate School Core Curriculum: Mouse Genetics 1 & 2.
Lecturer. Fall 1998, Spring of 1999-2006.
Med. Sciences 600: Graduate School Core Curriculum: Tumor Suppressors. Lecturer
and discussion leader. Spring 1999-2006
Interdisciplinary: Advanced Topics: Eukaryotic Cell Cycle. Lecturer and discussion
leader. Spring 2000, 2002, 2004.
Cell Biology 720: Advanced Topics: Tumor Biology. Course Organizer and Lecturer.
Fall 2002, 2004, 2006.

Service as an Advisor

Cynthi Guidi, 1998-2003. The Swi/Snf subunit Ini-1 in development and
cancer.— co-advisor with A. Imbalzano-, Ph.D. student - Department of Cell
Biology. (*currently a postdoctoral fellow with Dave Allis at the University of
Virginia*)

Heather Steinman, 1998-2004. p53-dependent and p53-independent roles for Mdm2 in tumorigenesis. Ph.D. student - Department of Cell Biology.
(*present position: Case Manager in the Office of Commercial Ventures and Intellectual Property at UMASS Medical School*)

Dr. Hayla Sluss, 1999-2005. Analysis of p53 modifications in mice. Postdoctoral fellow -*recipient of an NIH- NRSA postdoctoral fellowship. (present position: Assistant Professor, Department of Cancer Biology, UMASS Medical School)*

Dr. Irene Rainville, 2002-2005. Chromatin remodeling in Rb and p53 tumor suppression. Postdoctoral fellow (*present position: Medical Scientist- Correlagen, Inc. Cambridge MA*)

Dr. Huiling Liang, 2000-2005. Wnt5a in regulation of B-cell development and lymphoma. Instructor. (*present position: Director of Transgenic Research, Charles River Laboratories, Cambridge MA*)

Andrew Coles, 2003-present. Ing family members as mediators of p53 activity. Ph.D. student - Department of Cell Biology

Dr. Zdenka Matijasevic, 2004-present. MdmX mediated regulation of cell cycling. Research Assistant Professor - Department of Cell Biology.

Dr. Rajini Mudhasani, 2005-present. Dicer in p53 tumor suppression and diabetes. Postdoctoral fellow- Department of Cell Biology.

Dr. Xiaoxiong Shen, 2006-present. Mdm2-p53 signaling in skin homeostasis. Research Assistant Professor - Department of Cell Biology.

Departmental and University Service

Founder and Director, UMASS Transgenic Animal Modeling Core 1997 - present.
Organizer and Host, Program in Genetics Seminar Series 1997 - 2001.
Co-Founder and Organizer, Cell Cycle and Cancer Data Club 1998 - present.
Member, Institute Animal Care and Use Committee (IACUC) 1998 - present.
Member, Research Information Services Steering Committee 1998 - 1999.
Member, Cell Biology Department Graduate Committee 1999 - present.
Member, Lazare Research Building Vivarium Design Committee 1999 - 2000.
Vice-Chair- IACUC Facilities Subcommittee 2000 - present
Member, Faculty Search Committees - Program in Gene Function and Expression, Cancer Center, Molecular and Genetic Epidemiology, Gastrointestinal Cancer (Medicine); 1999 - 2002. Department of Animal Medicine
Director Search Committee 2001 - 2002. Department of Cancer Biology

Search Committee 2002 - 2004. Department of Cell Biology Search
Committee 2003 – present

Previous Grant Support

The Role of Mdm2 and p53 in Cell Growth and Tumorigenesis (RO1 CA077735).
12/99-12/03, National Institutes of Health (NCI). (S. Jones -PI). Yearly direct costs
= \$179,000. *Supplement for 2002 and 2003* = \$30,000.

Stem Cell Plasticity after Blastocyst Implantation (RO1 NS047839). 11/01-10/04,
National Institutes of Health (L Recht- PI, S Jones co-PI). Yearly direct costs =
\$214,000.

Nuclear Structure and Gene Expression (PO1CA082834). 12/00-01/06, National
Institutes of Health (G. Stein- PI, S. Jones- Collaborator). Yearly direct costs =
\$836,914.

Current Grant Support

The Role of Mdm2 in Cell Growth and Tumorigenesis (RO1 CA077735).
1/04-12/08, National Institutes of Health (NCI). (S. Jones -PI). Yearly direct costs
= \$202,500.

The Role of Ini1 in Development and Tumor Suppression (RO1 CA095216).
5/02-4/07, National Institutes of Health (NCI). (S. Jones- PI). Yearly direct cost =
\$222,500.

Dicer and miRNA in adipocyte differentiation and fat metabolism (R21 DK073324).
10/05-9/07, National Institutes of Health (NIDDK). (S. Jones- PI), Yearly direct
costs = \$150,000.

Intranuclear Trafficking of Bone Transcription Factors (PO1AR039588).
5/03-4/07, National Institutes of Health (G. Stein- PI, S Jones- Investigator).

Diabetes and Endocrinology Research Center (Center Grant: DK32520).
12/04-12/10, National Institutes of Health (A. Rossini- PI, S. Jones- Core
Director).

Publications (67 total, excluding abstracts)

Tibbetts, C., Larson, P.L. and Jones, S.N. (1985). Autoregulation of adenovirus E1A gene
expression. **J. Virol.** 57: 1055-1064.

- Jones, S.N. and Tibbetts, C. (1989). Upstream DNA sequences determine different responses of the adenovirus types 5 and 3 E1A promoters. **J. Virol.** 63: 1833-1838.
- Scarpa, M., Jones, S.N. and Caskey, C.T. (1989). Advances toward gene therapy. **Current Opinion in Pediatrics** 1: 453-464.
- Jones, S.N., Grompe, M., Munir, M.I. and Caskey, C.T. (1989). Germ line correction of OTC deficiency in *spf* mice. In: **Biotechnology and Human Genetic Predisposition to Disease**, UCLA Symposia on Molecular and Cellular Biology (Cantor, C.R. et al., eds.) Vol. 126, pp 95-107, Wiley-Liss, New York.
- Jones, S.N., Grompe, M., Munir, M.I., Veres, G., Craig, W.J. and Caskey, C.T. (1990). Ectopic correction of OTC deficiency in sparse fur mice. **J. Biol. Chem.** 265: 14684-90.
- Cournoyer, D., Scarpa, M., Jones, S.N. Moore, K.A., Belmont, J.W. and Caskey C.T. (1990). Gene therapy: A new approach for the treatment of genetic disorders. **Clin. Pharm. Therapeutics** 47: 1-11.
- Grompe, M., Jones, S.N. and Caskey, C.T. (1990). Molecular detection and correction of ornithine transcarbamylase deficiency. **Trends in Genetics** 6: 335-339.
- Jones, S.N., Jones, P.G., Ibarra, H., Caskey, C. T., and Craig, W.J. (1991). Induction of the *Cyp1a-1* dioxin-responsive enhancer in transgenic mice. **Nucleic Acids Res.** 19: 6547-51.
- Grompe, M., Mitani, K., Lee, C.C., Jones, S.N. and Caskey, C.T. (1991). Gene therapy in man and mice: adenosine deaminase deficiency, ornithine transcarbamylase deficiency, and duchenne muscular dystrophy. In: **Purine and Pyrimidine Metabolism in Man** (Elion, G.B., Harkness, R.A. and Zollner, N. eds.) Vol. VII, Plenum, New York.
- Coogan, J., Jones, S.N., Hall, R. and Tibbetts, C. (1992). Functional diversity of E1A gene autoregulation among human adenoviruses. **J. Virol.** 66: 3833-45.
- Gelb, B.D., Adams, V., Jones, S.N., Griffin, L.D., MacGregor, G.R. and McCabe, E.R.B. (1992). Targeting of hexokinase 1 to liver and hepatoma mitochondria. **Proc. Natl. Acad. Sci. USA.** 89: 202-206.
- Grompe, M., Jones, S.N., Lousched, H. and Caskey, C.T. (1992). Retroviral-mediated gene transfer of human ornithine transcarbamylase into primary hepatocytes of *spf* and *spf-ash* mice. **Human Gene Therapy** 3: 35-44.
- Jones, S.N., Roe, A.E., Donehower, L.A. and Bradley, A. (1995). Rescue of embryonic lethality in Mdm2 deficient mice by absence of p53. **Nature** 378: 206-208.

Rizwan, H., Cogan, J.D., Jones, S.N., and Tibbetts, C. (1995). Phenotypic determinants of adenovirus E1A gene autoregulation: Variable region between conserved coding domains 2 and 3. **Virology** 213: 666-670.

Jones, S.N., Donehower, L.A., and Bradley, A. (1995). Analysis of tumor suppressor genes using transgenic mice. **Methods: A Companion to Methods in Enzymology** 8: 247-258.

Ansari-Lari, M.A., Jones, S.N., Timms, K.M., and Gibbs, R.A. (1996). Improved ligation-anchor PCR strategy for identification of 5' ends of transcripts. **Biotechniques** 21: 34-38.

Jones, S.N., Ansari-Lari, M.A., Hancock, A.E., Jones, W.J., Gibbs, R.A., Donehower, L.A. and Bradley, A. (1996). Genomic organization of the mouse double minute 2 gene (*Mdm2*). **Gene** 175: 209-213.

Jones, S.N., Sands, A., Hancock, A.E., Vogel, H., Donehower, L.A., Linke, S.P., Wahl, G.M. and Bradley, A. (1996). The tumorigenic potential and cell growth characteristics of p53-deficient cells are equivalent in the presence or absence of Mdm2. **Proc. Natl. Acad. Sci. USA**. 93: 14106-14111.

Kubbutat, M.H.G., Jones, S.N. and Vousden, K.H. (1997). Regulation of p53 stability by Mdm2. **Nature** 387: 299-303.

Shi, Y.-P., Venkatachalam, S., Jones, S.N., Vogel, H., Bradley, A., Pinkel, D. and Donehower, L. A. (1998). Retention of the wild type p53 allele in tumors from p53 heterozygous mice: Is p53 an exception to the two hit hypothesis? **EMBO J.** 17: 4657-4667.

Jones, S.N., Hancock, A.E., Vogel, H., Donehower, L.A. and Bradley, A. (1998). Overexpression of Mdm2 in transgenic mice reveals a p53-independent role for Mdm2 in tumorigenesis. **Proc. Natl. Acad. Sci. USA**. 95: 15608-15612.

Fuchs, S.Y., Adler, V., Buschmann, T., Yin, Z., Wu, X., Jones, S.N. and Ronai, Z. (1998). JNK targets p53 ubiquitination and degradation in nonstressed cells. **Genes & Dev.** 12: 2658-2663.

Yamaguchi, T., Bradley, A., McMahon, A.E. and Jones, S. (1999). A Wnt5a pathway underlies outgrowth of multiple structures in the vertebrate embryo. **Development** 126: 1211-1223.

Tournier, C., Hess, P., Yang, D.D., Xu, J., Turner, T.K., Nimnual, A., Bar-Sagi, D., Jones, S.N., Flavell, R.A., and Davis, R.J. (2000). Requirement of JNK for stress induced activation of the cytochrome c-mediated death pathway. **Science** 288: 870-874.

Drissi, H., Luc, Q., Shakoori, R., Chuva de Sousa Lopes, S., Choi, J-Y., Terry, A., Hu, M., Jones, S.N., Neil, J.C., Lian, J.B., Stein, J.L., vanWijnen, A.J., and Stein, G.S. (2000). Transcriptional autoregulation of the bone related CBFA1/RUNX2 gene. **J. Cell. Phys.** 184: 341-350.

Guidi, C., Turner, T., Smith, T., Zambowski, B., Sands, A.S., Imbalzano, T., and Jones, S.N. (2001). Disruption of *Ini1* leads to peri-implantation lethality and tumorigenesis in mice. **Mol. Cell. Biol.** 21:3598-3603.

Tournier, C., Dong, C., Turner, T.K., Jones, S.N., Flavell, R.A., and Davis, R.J. (2001). MKK7 is an essential component of the JNK signal transduction pathway activated by pro-inflammatory cytokines. **Genes & Dev** 15:1419-1426.

Whitmarsh, A.J., Kuan, C-Y., Kennedy, N., Kelkar, N., Yaydar, T., Mordes, J.P., Appel, M., Rossini, A., Jones, S.N., Flavell, R.A., Raskic, P., and Davis, R.J. (2001). Co-ordination of the JNK signaling pathway by the MAPK scaffold JIP1. **Genes & Dev** 15:2421-2431.

Choi, J-Y., Pratap, J., Javed, A., Zaidi, S.K., Xing, L., Balint, E., Dalamangas, S., Boyce, B., van Wijnen, A.J., Lian, J.B., Stein, J.L., Jones, S.N., and Stein, G.S. (2001). Sub-nuclear targeting of the Runx/Cbfa/AML factors is essential for tissue-specific differentiation during embryonic development. **Proc. Natl. Acad. Sci. USA.** 98: 8650-8655.

Tyner, S.D., Venkatachalam, S., Choi, J., Jones, S., Ghebranious, N., Igelmann, H., Lu, X., Soron, G., Cooper, B., Brayton, C., Karsenty, G., Bradley, A., and Donehower, L.A. (2002) p53 mutant mice that display early ageing-associated phenotypes. (2002). **Nature** 415: 45-53.

Guidi, C.J., Jones, S.N., and Imbalzano, A.N. (2002). *Ini1* is essential for embryonic development and tumor suppression **Chemtracts: Mol.Biol & Biochem.** 14:751-756..

Steinman, H., and Jones, S.N. (2002). Generation of an Mdm2 conditional allele in mice. **Genesis** 32:142-144.

Luong, M.X., van der meijden, C.M., Hesselton, R., Monuki, E.S., Jones, S.N., Lian, J., Stein, J.L., Stein, G.S., Neufeld, E.J., and van Wijnen, A.J. (2002). Genetic ablation of the *CDP/Cux* protein C terminus results in hair cycle defects and reduced male fertility. **Mol. Cell Biol.** 22:1424-1437.

Li, L., Salmonsens, R.A., Turner, T.K., Litofsky, N.S., DiCristofano, A., Pandolfi, P.P., Jones, S.N., Recht, L.D., and Ross, A.H. (2002). PTEN in neural precursor cells: regulation of migration, apoptosis, and proliferation. **Mol. Cell. Neurosci.** 20:21-29.

- Rogoff, H.A., Pickering, M.T., Debatis, M.E., Jones, S.N. and Kowalik, T.F. (2002). E2F1 Induces Phosphorylation of p53 that is Coincident with p53 Accumulation and Apoptosis. **Mol. Cell Biol.** 22:5308-5318
- Schonoff, C.M., Daou, M.C., Jones, S.N., Schiffer, C.A., and Ross, A.H. (2002). Nitric oxide mediated inhibition of Hdm2-p53 binding. **Biochemistry** 41:13570-13574.
- Sluss, H and Jones, S.N. (2003). Analyzing p53 tumor suppressor functions in mice. **Expert Opinion on Therapeutic Targets** 7: 89-99.
- Jones, S.N. and Donehower, L.A. (2002). Functional analysis of tumor suppressor genes in mice. *Book chapter in* **Methods in Molecular Medicine: Tumor Suppressor Genes** (ed. W. El-Deiry) Humana Press USA. 223:283-314.
- Kennedy, N.J., Sluss, H.K., Jones, S.N., Bar-sagi, D., Flavell, R.A., and Davis, R.J. (2003). Suppression of Ras-stimulated transformation by the JNK signal transduction pathway. **Genes & Dev.** 17: 629-637.
- Houghtaling, S., Timmers, C., Noll, M., Reifsteck, C., Olson, S., Finegold, M., Jones, S., Meyn, S. and Grompe, M. (2003). Epithelial cancer in Fanconi Anemia D2 (Fancd2) knockout mice. **Genes & Dev.** 17:2021-2035.
- Moore, L., Venkatachalam, S., Vogel, H., Watt, J., Wu, C.-L., Steinman, H., Jones, S.N., and Donehower, L.A. (2003). Cooperativity of p19(Arf), Mdm2, and p53 in murine tumorigenesis. **Oncogene** 22:7831-7837.
- Liang, H., Chen, Q., Coles, A., Anderson, S., Pihan, G., Gerstein, R., Jureceic, R., and Jones, S.N. (2003). Wnt5a inhibits B cell proliferation and functions as a tumor suppressor in hematopoietic tissue. **Cancer Cell** 4:349-360.
- Steinman, H., Sluss, H.K., Pihan, G., Sands, A., and Jones, S.N. (2004). Absence of p21 partially rescues Mdm4 loss and uncovers an anti-proliferative effect of Mdm4 on cell growth. **Oncogene** 23:303-306.
- Steinman, H., Burstein, E., Lengner, C., Gosselin, J., Pihan, G., Duckett, C.S. and Jones, S.N. (2004). An alternative splice form of Mdm2 induces p53-independent cell growth and tumorigenesis. **J. Biol. Chem.** 279:4877-4886.
- Sluss, H.K., Armata, H., Gallant, J., Zhu, Z., and Jones, S.N. (2004). Phosphorylation of serine 18 regulates distinct p53 functions in mice. **Mol. Cell Biol.** 24:976-984.

Guidi, C.J., Veal, T., Jones, S.N., and Imbalzano, A.N. (2004). Transcriptional compensation for loss of an allele of the *Ini1* tumor suppressor. **J. Biol. Chem.** 279:4180-4185.

Rogoff, H., Pickering, M.T., Frame, F., Sanchez, Y., Jones, S., and Kowalik, T. (2004). Apoptosis associated with deregulated E2F activity is dependent on E2F1 and ATM/Nbs1/Chk2. **Mol. Cell Biol.** 24:2968-2977.

Doan, D.N., Veal, T.M., Yan, Z., Wang, W., Jones, S.N., and Imbalzano, A.N. (2004). Loss of the *Ini1* tumor suppressor does not impair the expression of multiple Brg1-dependent genes or the assembly of Swi/Snf enzyme. **Oncogene** 23:3462-3473.

Cha, K., Douglas, K., Potok, M.A., Liang, H., Jones, S.N., and Camper, S. (2004). Wingless signaling affects pituitary gland shape. **Mech Dev.** 121:183-194.

Greco, B., Low, H.P., Johnson, E.C., Salmonsem, R.A., Gallant, J., Jones, S.N., Ross, A.H., and Recht, L.D. (2004). Differentiation Prevents Assessment of Neural Stem Cell Pluripotency after Blastocyst Injection. **Stem Cells** 22:600-608.

Liang, H., Atkins, H., Abdel-Fattah, R., Jones, S.N. and Lunec, J. (2004). Genomic organization of the human MDM2 oncogene and its relationship to alternatively spliced mRNAs. **Gene** 338:217-223.

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EXHIBIT B TO THE
DECLARATION OF STEPHEN N. JONES, PH.D.

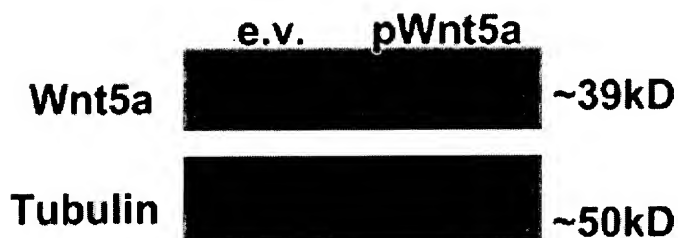


Figure A

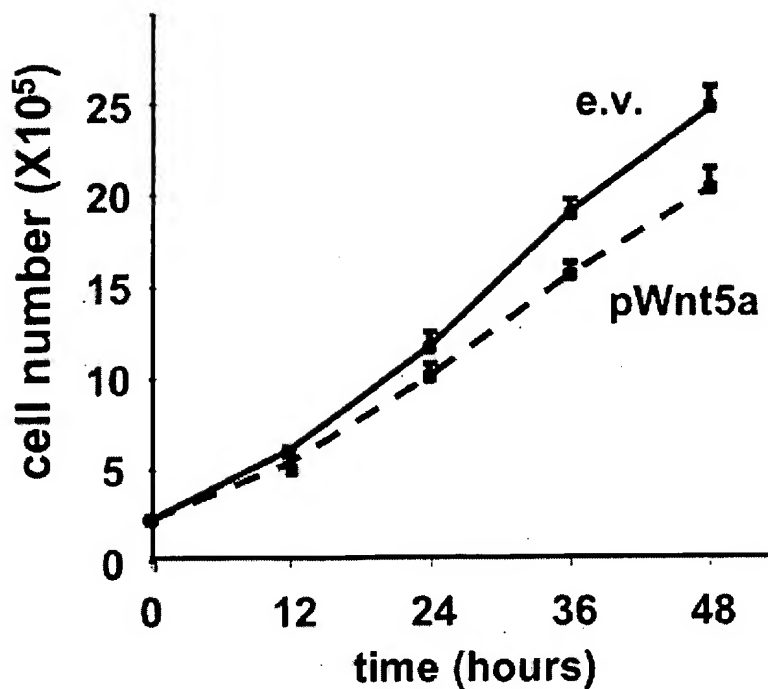


Figure B



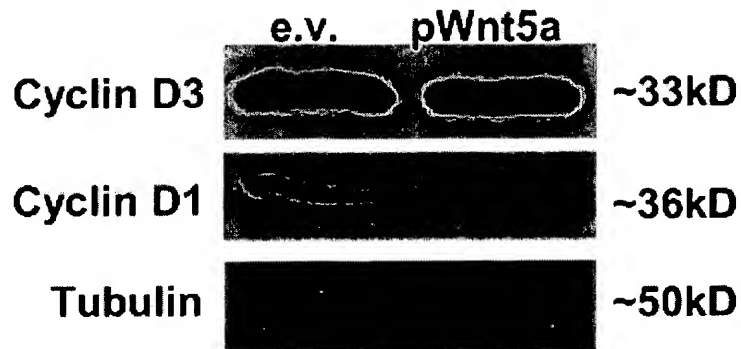


Figure C

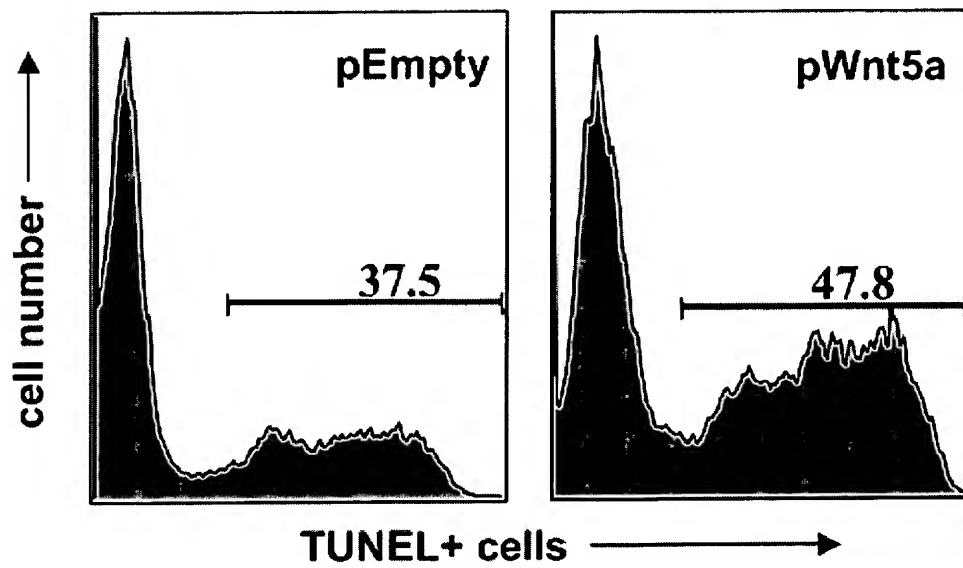


Figure D

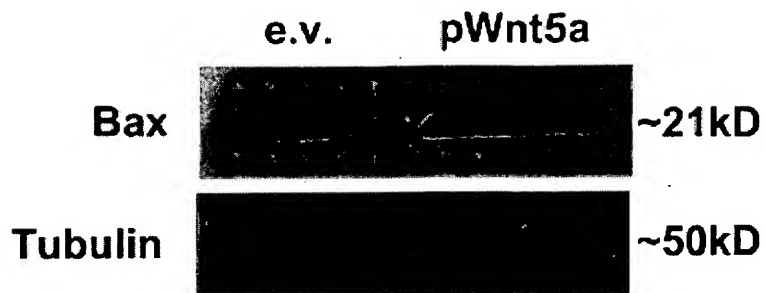


Figure E

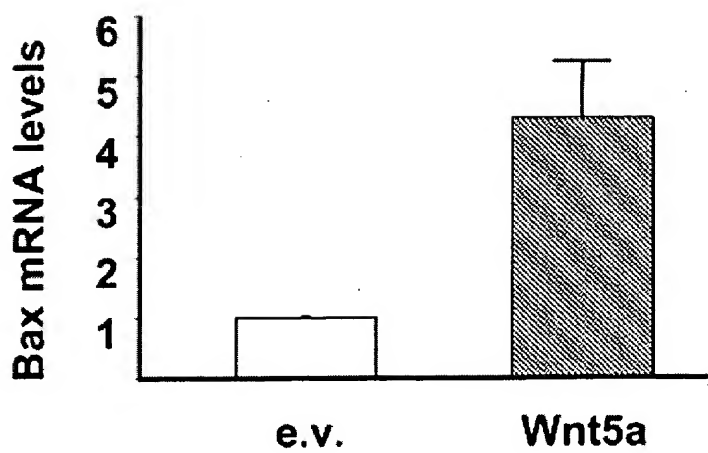


Figure F

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